OBJECTIVES: This research will present the Bayesian decision analytic framework for late phase study simulation and calculation of chance of study success applied to optimal target population and study design. A real-world example in mother-to-child transmission of HIV conducted in Thailand will be used to illustrate the concepts throughout. **METHODS:** Predictive models describing virtual cohorts over time under various care strategies can be informed via Bayesian inference using all relevant data available on associations between population characteristics, relative drug efficacy, drug uses and design parameters. In the proposed example, historical transmission data from 3,876 Thai women were modeled via mixed-effect logistic regression adjusted for viral load, gestational age, CD4 count at delivery and infant treatment duration. Viral load was described as an exponential function of prophylaxis duration. Monte Carlo simulations were used to predict *intrapartum* transmission rates with and without single dose nevirapine (sdNVP) added to the standard of care (antenatal prophylaxis), and predict chance of success of a naturalistic Phase IIIb study in Thailand under various assumptions on target population and adaptive study design. **RESULTS:** In women with short prophylaxis durations (<8-weeks) estimate of *intrapartum* transmission rate was 2.6% (95%-Credibility Interval=0.5%-9.2%) with the standard of care and 0.8% (95%-CI=0.1%-2.9%) with sdNVP added to standard care, corresponding to a risk ratio of RR=3.9 (95%-PI=2.1-9.7). Study simulations showed that a single-arm study with stopping rules at N=58, 118, 275, and 410 has 78% (resp. 68%) probability of evidencing RR>1.3 (resp. RR>2). **CONCLUSIONS:** When the association between outcomes, design parameters and the main effectiveness drivers can be informed by historical data, Bayesian predictive models can be powerful decision support tools for optimal target population and late-phase or pragmatic study design.

PRM22

THE STATISTICAL ANALYSIS OF DELAYED EFFECTS IN SURVIVAL OUTCOMES FOR IMMUNOTHERAPIES. ESTIMATION OF TIME-DELAY AND APPLICATION OF WEIGHTED LOG RANK

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OBJECTIVES: The aim of the study was to assess the delayed-time effect on survival of the immunotherapy with a cancer vaccine by comparing the conventional logrank test vs a weighted logrank in presence of non-proportional hazards. **METHODS:** Data from a multicenter, open-label and randomized phase III clinical trial with an EGF-based cancer vaccine in advanced NSCLC. The diagnosis of the delayed-time effect was done and the time-delay was estimated. The non-proportional hazards were also confirmed and tested delayed effect on survival of the treatment. Weighted logrank tests was applied and the results were compared with those obtained using the conventional logrank test. The R software was used in the analysis. **RESULTS:** The time-delay was estimated in 28 months and a significant effect after this time was verified. The proportional hazard assumption was not satisfied. The median survival for the vaccinated arm was 10.37 months vs. 8.93 months for non-vaccinated arm. The difference was statistically significant by weighted logrank (p=0.04) and the conventional logrank test does not detect this difference. **CONCLUSIONS:** Weighted logrank is substantially more efficient than the conventional logrank statistic in those situations in which non-proportional hazards are foreseen. This analysis is recommended for immunotherapies where the appearance of a late biological effect is displayed several months after randomization.

PRM23

IMPACT OF SINGLE RISK FACTOR CHANGES ON LONG TERM OUTCOMES AND COST IN A TYPE 2 DIABETES MODELING STUDY CONTRASTING PROJECTIONS WITH UKPDS 68 VERSUS UKPDS 82 RISK EQUATIONS

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OBJECTIVES: The degree to which predefined risk factor (RF) changes alter long-term clinical and cost outcomes in the IMS-CORE-Diabetes-Model (CDM) was reported in earlier publications. Since this time the CDM has undergone a series of updates including the inclusion of recently published UKPDS-82 risk equations (UK-82-RE). The objective of this study was to project the lifetime benefits and total lifetime costs (TLC) associated with a range of selected RF changes opposing results from CDM projections utilizing UKPDS-68 risk equations (UK-68-RE) vs. UK-82-RE. **METHODS:** The CDM was applied to project the lifetime benefits (life years (LYs), quality adjusted life years (QALYs)) and TLC (£GBP) associated with baseline RF changes for HbA1c, body-mass-index (BMI), systolic blood pressure (SBP), high-density-lipoprotein (HDL) and low-density-lipoprotein (LDL). A intermediate risk type-2 diabetes cohort (age 52 years, HbA1c 8%, SBP 140 mm-Hg, BMI 30 Kg/m2, HDL 50 mg/dl and LDL 150 mg/dl) was projected over lifetime to explore the sensitivity of undiscounted LYs, QALYs and TLC for selected RF ranges (A1c+/-2%, SBP+/-20 mmHg, BMI+/-2 Kg/m^2, HDL+/-10 mg/dl, LDL+/-20 mg/dl). Linear regression models were fitted to assess the degree of end point sensitivity per unit RF change. **RESULTS:** When UK-68-RE were applied, projected changes in benefits were 0.264, 0.094, 0.050, -0.611 and 0.162 LYs and 0.288, 0.111, 0.123, -0.358, and 0.113 QALYs associated with unit RF reductions of 1% point (A1c), 10 mm-HG (SBP), 1 KG/m2 (BMI), 10 mg/dl (HDL) and 10 mg/dl (LDL), respectively. This compared to changes of 0.161, 0.079, 0.053, -0.262, 0.311 (LYs) and 0.215, 0.099,0. 116, -0.178, 0.208 (QALYs) utilizing UK-82-RE. TLC decreased by £1'105, £298, £115, £680 and £38 utilizing UK-68-RE and £1'073, £309, -£71, -£221, -£7 with UK-82-RE. **CONCLUSIONS:** The degree to which RF changes are translated into benefits and costs may change considerably dependent on the choice of selected risk equations.

PRM24

A CHART ABSTRACTION BASED METHOD TO CLASSIFY REAL WORLD PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION BASED ON WHO FUNCTIONAL CLASSIFICATION

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Retrospective database studies of PAH using US payer claims data have limitations due to lack of specific ICD-9 codes for PAH and ability to identify patient severity. Previous studies used an algorithm which includes patients with non-specific PH codes, along with a claim for an advanced PAH drug therapy. This study attempts to validate the algorithm and identify patient disease severity through linkage to data abstracted from medical charts. **OBJECTIVES:** To evaluate validity of a retrospective review of payer database along with chart abstraction for confirmation of PAH diagnosis and identification of World Health Organization Functional Class (FC). **METHODS:** Medicare patients who received an (1) endothelin-receptor antagonist, phosphodiesterase type 5 inhibitor, or prostacyclin AND (2) had a diagnosis of pulmonary hypertension, other chronic pulmonary hypertension or chronic pulmonary heart disease OR (3) medical claim indicating right heart catheterization (RHC) were identified from pharmacy and medical claims data. A random sub-sample of 110 patients was chosen and the providers contacted to provide medical charts. Charts were reviewed to abstract data indicating PAH diagnosis, FC, and/or symptoms, diagnostic tests, and treatments to enable classification. **RESULTS:** Of 110 charts requested, 41 were received and abstracted. Twenty-one charts (51%) came from a specialist. All 41 charts documented a confirmed diagnosis of PAH. Of those, 18 (44%) explicitly identified PAH class. Physical symptoms were reported, with dyspnea (66%) being most frequent, while walk test results, documentation of RHC and pulmonary diagnostic tests were reported in less than 20% of cases. **CONCLUSIONS:** The identification algorithm successfully identified diagnosed, confirmed cases of PAH. Refinements to provider selection algorithm could result in an increase in provider response rate, charts with documented FC and overall chart data quality.

PRM25

QUALITY ASSESSMENT OF CONTROLLED TRIALS EVALUATING CHINESE HERBAL MEDICINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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OBJECTIVES: We conducted a systematic review to appraise the methodological quality of controlled clinical trials evaluating the efficacy and safety of Chinese herbal medicine (CHM) patients with rheumatoid arthritis (RA). **METHODS:** We searched electronic databases (Medline, EMBASE, The Cochrane Library, and Web of Science) from inception until May 2014. Study selection was performed by 2 independent reviewers. The methodological quality of the trials was assessed using the Cochrane risk of bias tool for randomized trials and Newcastle Ottawa Scale for controlled non-randomized studies. **RESULTS:** 54 studies were included (51 randomized trials; 3 non-randomized studies) evaluating 7,792 patients. Only one study was conducted in the US, the remaining in China. There were 3,446 patients receiving CHM. In the control groups 2,283 patients received a disease modifying anti-rheumatic drug (DMARD), 182 non-steroidal anti-inflammatory drugs (NSAIDs), and 164 inert placebo. For the randomized studies, when evaluating selection bias 54% of the studies were judged to have an adequate random sequence generation, but 77% had inadequate allocation concealment. 79% had a high risk of performance bias (not blinding participants and/or personnel) and detection bias was unclear in 56% of the studies; 62% of the studies reported how missing data was handled, therefore attrition bias was judged to be low. In 87% no disclosure of interest or source of founding was reported. For non-randomized studies, all the studies were representative of RA patients, had an adequate ascertainment of intervention with comparable groups, but only one demonstrated that the outcome of interest was not present at start of study or provided the rate of lost to follow-up. **CONCLUSIONS:** Studies evaluating CHM often fail to meet expected methodological criteria, and high quality evidence is lacking. Future studies of CHM should be methodologically robust and adhere to reporting guidelines such as the CONSORT statement for TCM.

RESEARCH ON METHODS – Cost Methods

PRM26

VALIDATION OF THE HOSPITAL EPISODE STATISTICS OUTPATIENT DATASET IN ENGLAND

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OBJECTIVES: Health economists are being encouraged to use routine datasets for resource-use measurement and costing purposes in economic evaluations alongside clinical trials to reduce research burden. The Hospital Episode Statistics (HES) dataset, which records all NHS hospital-based activity in England, is one such dataset. However, its validity for research purposes has not been established. This study aims to assess the validity of the HES outpatient dataset. **METHODS:** Men who died of, or with, prostate cancer were selected from a prostate-cancer screening trial (CAP, Cluster randomised triAl of testing for Prostate cancer). Details of visits that took place after 1/4/2003 to hospital outpatient departments for conditions related to prostate cancer were extracted from medical records (MR). Data from the HES outpatient dataset were obtained for the same men. Appointments for visits extracted from MR were sought in the HES dataset. The matching procedure was repeated for periods before and after 1/4/2008 (when the dataset was accredited as a national statistic). **RESULTS:** 4922 outpatient appointments were extracted from MR for 370 men between 2003 and 2012. 4086 appointments recorded in MR were identified in the HES dataset (83.0%; 95%CI 81.9–84.1). Allowing a +/-2 day tolerance for the appointment date resulted in a slight improvement to 4171 (84.7%; 95%CI 83.7–85.7) matches (p=0.5). For appointments occurring when the dataset was considered experimental (prior to 1/4/2008), 2194/2754 (79.7%; 95%CI 78.1–81.2) matches were observed, while 1892/2168 (87.3%; 95%CI 85.8–88.6) appointments occurring after 1/4/2008 were identified (p=0.03). **CONCLUSIONS:** The HES outpatient data-